EMA/602814/2021
EMEA/H/C/005454

Rybrevant (*amivantamab*)

An overview of Rybrevant and why it is authorised in the EU

What is Rybrevant and what is it used for?

Rybrevant is a cancer medicine used to treat adults with advanced non-small cell lung cancer (NSCLC) whose cancer cells have certain genetic changes. These changes are in the gene for a protein that controls cell growth, epidermal growth factor receptor (EGFR), and are known as 'activating EGFR exon 20 insertion mutations'. The medicine is given when cancer treatment with platinum-based medicines has not worked well enough.

Rybrevant contains the active substance amivantamab.

How is Rybrevant used?

The medicine can only be obtained with a prescription. Treatment with Rybrevant should be started and supervised by a doctor who is experienced in using cancer medicines and given in a setting where any infusion-related side effects can be managed.

Rybrevant is given as an infusion (drip) into a vein. The first week's dose is split over two successive days, and then it is given once weekly for the next three weeks and after that once every two weeks. The dose of the medicine depends on the patient's bodyweight. Treatment is continued until the disease gets worse or side effects become too severe. Treatment should be stopped temporarily or permanently, and subsequent doses may be reduced if the patient experiences certain side effects.

Patients should be given antihistamines (allergy medicines), antipyretics (fever-reducing medicines), and corticosteroids before the first treatment to reduce infusion-related reactions. In the following treatment sessions, patients should be given antihistamines and antipyretics.

For more information about using Rybrevant, see the package leaflet or contact your doctor or pharmacist.

How does Rybrevant work?

In NSCLC cells, EGFR is often overactive, causing uncontrolled growth of cancer cells.

Amivantamab is a monoclonal antibody (a type of protein) designed to recognise and attach to two receptors (targets) on the surface of the NSCLC cells simultaneously. One part of the antibody attaches to EGFR with activating EGFR Exon 20 insertion mutations. The other part attaches to MET, a receptor

important for cancer growth and metastasis (cancer that spreads to another part of the body). By attaching to the two proteins, amivantamab blocks them from receiving the messages the cancer cells need for growing and spreading. The attached antibody also attracts and activates immune cells to kill the targeted cancer cells.

What benefits of Rybrevant have been shown in studies?

In one main study, Rybrevant was effective at reducing the size of the cancer in patients with NSCLC with activating EGFR exon 20 insertion mutations who had previously been treated with platinum-based cancer medicines. Rybrevant was not compared with any other treatment or placebo (a dummy treatment).

Response to treatment (shrinkage in size of the cancer) was assessed using body imaging. In around 37% (42 out of 114) of the patients, the cancer shrank after treatment with Rybrevant. On average, responses lasted for just over 12 months.

What are the risks associated with Rybrevant?

The most common side effects with Rybrevant (which may affect more than 1 in 5 people) are rash, infusion-related reactions, nail toxicity (nail abnormalities with pain or discomfort), hypoalbuminaemia (low blood levels of the protein albumin), oedema (fluid retention), tiredness, stomatitis (inflammation of the lining of the mouth), nausea (feeling sick), and constipation. The most common serious side effects (which may affect more than 1 in 100 people) are interstitial lung disease (disorders causing scarring in the lungs), infusion-related reactions and rash.

For the full list of side effects and restrictions of Rybrevant, see the package leaflet.

Why is Rybrevant authorised in the EU?

Patients with NSCLC with EGFR Exon 20 insertion mutations have few available treatment options if their cancer gets worse or does not respond to platinum-based therapy. Although the main trial included a relatively small number of patients and did not compare Rybrevant with another cancer treatment, it showed that the medicine can provide clinically significant benefits in a group of patients who have limited treatment options. Its side effects were considered manageable with appropriate measures, such as changing the dose or, for infusion-related reactions, modifying the infusion and treating the symptoms.

The European Medicines Agency, therefore, decided that Rybrevant's benefits are greater than its risks and it can be authorised for use in the EU.

Rybrevant has been given 'conditional authorisation'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Rybrevant?

Since Rybrevant has been given conditional authorisation, the company that markets Rybrevant will provide additional results from an ongoing study in patients with advanced or metastatic NSCLC with activating EGFR Exon 20 insertion mutations. The study will compare the effectiveness of adding Rybrevant to platinum-based chemotherapy versus platinum-based therapy alone for initial treatment.

What measures are being taken to ensure the safe and effective use of Rybrevant?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Rybrevant have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Rybrevant are continuously monitored. Suspected side effects reported with Rybrevant are carefully evaluated and any necessary action taken to protect patients.

Other information about Rybrevant

Rybrevant received a conditional marketing authorisation valid throughout the EU on 09 December 2021

Further information on Rybrevant can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/ rybrevant.

This overview was last updated in 12-2021.